The clinical diagnosis of vascular dementia

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ATTEMPT TO PURIFY THE NORMAL CELLULAR ISOFORM OF PRION PROTEIN FROM MOUSE AND HAMSTER BRAIN

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Recent developments in genetics and molecular biology of spongiform encephalophaties (prion diseases) confirm the key role of scrapie amyloid (prion) protein in susceptibility, disease transmission, incubation time and pathogenesis. The abnormal isoform of scrapie amyloid precursor (prion protein, PrP^{Sc}) is derived from a normal cellular protein (PrP^{C}) through a post-translational modification and/or conformational change. The conversion of PrP^{C} into Prp^{Sc} is a fundamental step in the pathogenesis, and therefore the comparison of PrP^{Sc} and PrP^{C} native conformations is essential to understand the molecular mechanism of prion-induced diseases.

PrP^{C} was enriched in mouse brain homogenate by differential centrifugations and extraction with Triton-X114. The resulting phospholipid-rich phase was digested by phosphatidylinositol-specific phospholipase C (PIPLC). Supernatants containing PIPLC-released PrP^{C} were separated by immobilized Cu^{++} ion affinity chromatography and cation exchange chromatography; a certain degree of purification was obtained but yields were low. Our results suggest that PIPLC-released PrP^{C} is not as hydrophilic as previous studies have suggested. Even after enzymatic cleavage of the glycolipid anchoring PrP^{C} to membranes, PrP^{C} tends to associate with phospholipids and to aggregate. Additional chromatographic steps in the presence of nondenaturing detergents are necessary to increase the yield of PrP^{C}.

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CRITERIA FOR DIAGNOSIS OF PURE ALZHEIMER'S DISEASE

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Today, the clinical diagnosis of Alzheimer's disease (AD) is made using exclusion criteria and symptomatological criteria that are not well defined. Markers for the underlying pathological processes are not taken into account. This involves a risk that the criteria delimit a heterogenous group of patients. The limit against vascular dementia in particular is poorly defined. We suggest a diagnosis made by weighing together the results of a symptom analysis called Stepwise Comparative Status Analysis (STEP) and evidence provided by various biological markers. We have been able to identify two types of AD. AD type I or 'pure' AD is characterized by a cortical degeneration of neurons and their synapses. AD type II, or 'senile dementia of the Alzheimer type', is characterized by several different types of pathological processes, not only the cortical degeneration typical of AD type I, but also vascular changes, e.g. white-matter lesions. For 'pure' AD we have worked out diagnostic criteria that are currently in press. In short, these criteria include presence of instrumental deficits and memory disturbances and absence of significant radiologically detectable white-matter lesions. It is our hope that these more specific AD criteria that take into account the underlying pathological processes will be used in clinical drug trials and in pathophysiological AD research.

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THE CLINICAL DIAGNOSIS OF VASCULAR DEMENTIA:
A COMPARISON BETWEEN SEVEN CURRENTLY USED DIAGNOSTIC CRITERIA.

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Since the introduction of the Ischemic Scale (IS) of Hachinski et al. in 1974, several clinical criteria for the differentiation between Alzheimers disease (AD) and Vascular dementia (VaD) have been proposed. These are: the modified IS of Rosen et al. (1980) and of Loeb (1983), those outlined by DSM-III (-R) (1980) and Erkinjuntii et al. (1987), and the recent consensus-criteria of the ADDTC (Chui et al., 1992) and of the NINDS-AIREN (Román et al., 1993). In the present study, we applied these seven difeerent sets of criteria for VaD to a sample of demented outpatients visiting the Maastricht Memory Clinic, in order to compare prevalence rates, and to investigate the level of (dis)agreement between the criteria.

The data of 109 consecutively referred patients (mean age 70.1 yrs.) with mild to moderate dementia were evaluated. Patients with somatic or psychiatric disorders other than primary degenerative of cerebrovascular disorders were excluded from this study.

The percentage of patients diagnosed as VaD varied between 33% -using the IS of Rosen et al.- and 7%, according to the NINDS-AIREN criteria. The percentage of patients diagnosed as AD ranged between 54-75% -using the DSM-III-R or the NINDS-AIREN criteria for the *exclusion* of VaD respectively. Depending of the criteria used, the percentage of unclassified patients ranged from 2-32%. The agreement with regard to the diagnosis of VaD between the different criteria was only slight to modest (overall kappa: 0.48), whereas the agreement with regard to the diagnosis of AD was substantial (overall kappa: 0.71).

We conclude that the prevalence of VaD depends to a large extent on the criteria that have been used. For the exclusion of VaD for the diagnosis of AD, the choice is much less critical.

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DEMENTIA DIAGNOSIS IN PRIMARY CARE: RESULTS OF A REPRESENTATIVE SURVEY IN SOUTHERN LOWER SAXONY, GERMANY. J. Staedt, G. Stoppe, H. Sandholzer*, S. Winter, J. Kiefer, M. Kochen*, E. Rüther. Depts. of Psychiatry and General Practice*, University of Goettingen, 37075 Goettingen, Germany.

Since primary care physicians play the most important role for diagnosis and therapeutic management (at least in the early phase) of patients with senile dementive disorders, we performed a survey to investigate on diagnostic accuracy.

We used two case vignettes, each describing a 70year old widow complaining memory problems. In case I these problems were slight and unspecific, in case II there were typical histories and characteristics of moderate dementia of either Alzheimer's type (SDAT; IIb) or Multi - infarct - type (MID; IIa)). In addition case I had no cerebrovascular risk factors, whereas case 2 had. These case vignettes were randomly assigned to 145 general practitioners and 14 neuropsychiatrists in primary care (response rate overall 83.2%). Trained interviewers asked for diagnostic and differential diagnostic considerations.

Main results are: Impairment of cerebral blood flow was considered most frequently to be the cause of the disorder, independently from the presence of cerebrovascular risk factors. SDAT was correctly diagnosed in 25.9% in case IIb, MID was diagnosed in 37.2% in case IIa. Adverse drug effects were considered for (differential) diagnosis only by a minority of the physicians (1.9%). In case I, 57.8% of the physicians considered depression for diagnosis or differential diagnosis with the neuropsychiatrists doing that significantly more often (78.6% for differential diagnosis) than the general practitioners.

In conclusion, dementia is widely underdiagnosed in primary care. Cerebrovascular mechanisms are conceptualized as main reasons for dementia. Education in primary care should also focus on the fact, that treatable causes of dementia like adverse drug effects and depression are underdiagnosed, which may have major consequences on health care in old age. It would be interesting to replicate this study in other countries with other education and health care systems.

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THE COGNITIVE BATTERY FOR DEMENTIA IN THE DIAGNOSIS OF ALZHEIMER'S DISEASE. K.J. Christensen, J.R. McCarten, S.J. Rottunda, and B.E. Riley. Geriat. Res. Educ. Clin. Ctr., VA Med. Ctr., and Depts. of Neurology and Psychology, University of Minnesota, Minneapolis, MN 55417 USA.

The purposeof this study was to determine whether profile analysis using the Cognitive Battery for Dementia (CBD) can improve diagnostic accuracy in Alzheimer's disease (AD). The CBD was developed to provide reliable measurement of six cognitive abilties throughout the performance range of moderately severe dementia patients to healthy older adults. Profile analysis provides a quantitative means of evaluating the similarity of an individual patient's pattern of cognitive test results to that of the average pattern seen in patients with probable AD. In an initial study of 31 patients with antemortem diagnoses of probable AD, four patients had cognitive profiles that were